



KAWASAKI, JAPAN

A city of dynamic changes

With its strong manufacturing technology base linked to a worldwide transportation network, Kawasaki is fast becoming a city of innovation.

With a venerable 100-year-old history of manufacturing that has bolstered Japan's industrial growth, Kawasaki is a city on the cusp of extraordinary change, drawing on its accumulated knowledge and expertise in industry and technology to forge ahead with new successes in the life sciences and environmental engineering sectors.

During the past 100 years of Japan's economic growth, in particular the post-World War II era, the Keihin Industrial Zone has played a pivotal role in the rise of many of the nation's leading corporations in the manufacturing industries. Today, the Keihin Industrial Area, covering a total area of approximately 4,500 hectares that stretches south along a belt of land from Tokyo to Yokohama, still serves as one of Japan's major clusters of manufacturing activities, with Kawasaki City as its heart.

Kawasaki City is a vibrant metropolis of 1.4 million people, and one of the main cities forming

the Greater Tokyo Area, along with Tokyo, Kanagawa, Chiba, and Saitama in the surrounding Kanto region. Located on the south bank of the Tama River, Kawasaki City has excellent connections by land, sea and air, with convenient access to Haneda Airport (Tokyo International Airport) that serves as a major domestic and international gateway.

The historical transition between Japan's traditional and modern manufacturing industries remains much in evidence in Kawasaki City, where the well-connected seafront and landfill areas provide suitable bases for large ship-building factories, iron and non-ferrous metal production factories, as well as petrochemical and refinery industries. Numerous factories were built and towns had taken shape around the factories by the middle of the 20th century. After World War II, landfill was promoted as a way to build the industrial complex that formed the foundations of the petrochemical industry, which in turn powered the Japanese economy.

Over the years, the seafront has undergone several phases of redevelopment. Today, Kawasaki is an important base of energy resources supporting the power demands of the wider metropolitan area. Thermal power



The vicinity of Haneda Airport, situated across the Tama River, is of major strategic importance for the Kawasaki region.

plants developed in the area boast world-class technologies and efficiency, and there are companies that produce geothermal facilities and develop large-capacity storage batteries. Renewable energy sources using biomass, solar, and wind energy are also on the rise. Recycling and the adoption of low-carbon technologies and inter-business steam heat transfer systems are also key activities leading to the development of an eco-industrial complex on the seafront. In addition, there are plans to transform Kawasaki into a 'smart' city that showcases new environmental engineering products and techniques.



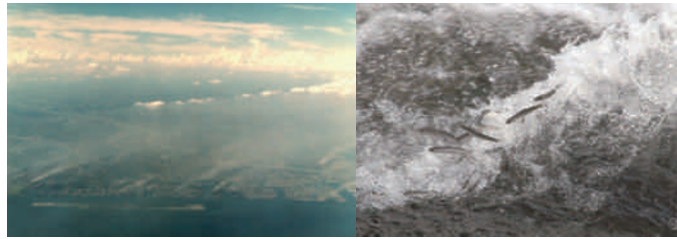
Accumulation of knowledge and expertise

Over the years, Kawasaki has steadily built on its multilayered, dynamic structure that is exceptionally well-suited to shortening the gap between high-quality basic research and practical applications, with its numerous research and development institutions and corporations keen to tap into this knowledge base. These developments are supported by the solid experience of a long-standing manufacturing industry capable of producing the chemicals and metals required to create prototypes, as well as developing advanced machinery and electronic products. Kawasaki has all of the fundamental benefits and infrastructure for *Monozukuri*, Japanese manufacturing that encompasses all aspects from design to production. By amassing a wealth of knowledge and attracting top intellectual talent to the area, Kawasaki is superbly positioned to match and translate research seeds to the needs of industry in the form of applied technologies, prototypes, and mass production.

Kawasaki City is home to nine universities, including Meiji University, St. Marianna University Medical School, and Nippon Medical School, and in the Greater Tokyo Area there are currently 35 universities and graduate schools with science and technology departments offering post-graduate courses. In total there are more than 200 research and development (R&D) and major educational institutions situated within the Kawasaki region — a formidable hub of research activity that enables outstanding opportunities for basic research to be translated into cutting-edge applications.



Iris garden at Ikuta Ryokuchi Park.



Left: The sky over Kawasaki in the 1960s. **Right:** A school of ayu, or sweetfish, swimming up the Tama River after environmental restoration.

Additionally, the numerous R&D links between industry and academia enable manufacturers to obtain critical feedback on prototypes from academic experts and end-users.

It is hardly surprising, therefore, that many of Japan's leading businesses including Toshiba, Fujitsu, NEC, Hitachi, Canon, Showa Denko, JFE, Ajinomoto, and Suntory, as well as Japanese subsidiaries of global companies, have turned to Kawasaki as their location of choice to set up R&D bases and facilities. Recognising the major R&D benefits of the region, there are currently also 41 foreign firms that have established business bases in Kawasaki.

The Kawasaki region is also renowned for its three science parks — Kanagawa Science Park, Shin-Kawasaki Forest of Creation, and Techno Hub Innovation Kawasaki — as well as an R&D industrial park, the Kawasaki Microcomputer (MICOM) City, located in the southern Kurokawa region of Kawasaki.

By drawing on its combined strengths in research and manufacturing, mobilizing science and technology-based enterprises, and furthering developments in medicine, biotechnology, physics, chemistry, and engineering, the Kawasaki region is making significant contributions to projects that aim to address critical issues and challenges such as the rapidly ageing society and sustainability.

In addition to undergoing a radical transformation in terms of industrial regeneration, Kawasaki is also focusing on exploring new areas of life sciences, as well as the fast-growing and exciting field of environmental engineering.

Many of the technologies that formed such an important basis for the development of Japan's machinery, electronics, and chemical engineering industries are now also finding new applications in healthcare and environmental sciences.

Rediscovery and rejuvenation

Just 90 kilometers west of Kawasaki, Mount Fuji stands majestically as an enduring symbol of Japan. During the post-war period of rapid economic growth, however, views of Mount Fuji were obscured due to the high levels of industrial air pollution, which in turn led to soil contamination, water pollution, and noise pollution. To address the growing problems of environmental pollution, Kawasaki became the first city to enforce a pollution control ordinance in 1960. The city's pioneering approach made it possible for Kawasaki to successfully overcome industrial pollution in the 1970s. One of the reasons why Kawasaki today has gained acclaim as a centre for environmental engineering is largely attributable to its history of overcoming industrial pollution and finding solutions to achieve the coexistence of residential and industrial zones. In 2008, Chinese president Hu Jintao visited Kawasaki's seafront area to learn from the city's experience.

During the period of Japan's high economic growth, the Tama River flowing between Kawasaki and Tokyo used to be polluted with effluent and floating garbage. However, following the enforcement of strict regulations, the water became so clean that today, schools of ayu, or sweetfish, swimming up the Tama River are a common sight.

The riverbank is now a place where local residents can relax and enjoy refreshing greenery in a metropolitan area. Ikuta Ryokuchi Park to the north and Todoroki Green Park in central Kawasaki also form an important part of the region's natural attractions.

Kawasaki is also well-known for its many cultural and historical attractions, with many facilities around the city demonstrating its unique culture, style and workmanship. Some of the city's most popular destinations include the Open-Air Folk House Museum (Nihon Minka-en) that displays fine examples of traditional Japanese architecture, the Muza Kawasaki Symphony Hall, the Fujiko F. Fujio Museum dedicated to the creator of the perennially popular cartoon, Doraemon series, and the Taro Okamoto Museum of Art, exhibiting the works of the internationally-renowned artist and sculptor born in Kawasaki City in 1911.



Night views of factories on the seafront.

Due to its direct and convenient access to the country's extensive railway and road networks, Kawasaki welcomes visitors all year round, who enjoy a wide range of activities stemming from the region's rich history, culture, commerce, and industry.

One of the clearest indications of Kawasaki's rejuvenation is its stunning nightscape that today is attracting younger crowds to the redeveloped seafront areas. Special night tours of Kawasaki by boat offer a fascinating glimpse of the past and present, as the city continues to evolve and become a hub of creativity and innovation.



CITY OF KAWASAKI



KAWASAKI CITY

Jet set for large-scale innovation

With the development of KING SKYFRONT (Kawasaki INnovation Gateway at SKYFRONT) — a large-scale strategic base for the advancement of science and technology situated on the opposite shore of Haneda Airport — Kawasaki is strengthening its foothold in innovative areas of research and development.

Kawasaki is fast establishing itself as a major innovation hub, drawing on its superb geographical location, formidable resources in industry and academia, and its strong manufacturing and technological roots. A new strategic base, KING SKYFRONT, is being built on an area covering 40 hectares in the Tonomachi District of Kawasaki, opposite Haneda Airport (Tokyo International Airport) across the Tama River. The base is designed to integrate research and development for a wide range of advanced technologies, including micro- and nanotechnologies, in order to address global issues through the life sciences and environmental fields.

The proximity of Haneda Airport, offering domestic and international flight services, is a major advantage for the development of KING SKYFRONT. Haneda began operation as Tokyo's original international airport in 1952 but was later overtaken in this role by Narita airport which was opened in 1978, 70km to the west of the capital. In the first decade of the 21st century, Haneda was redeveloped as part of a national initiative which saw the completion of a new international terminal in 2010 and has now regained its position as the principle international air hub for the Greater Tokyo area.

Strategies fit for the 21st century

The original grounds of the KING SKYFRONT project were home to the flourishing automotive and petroleum industries in the 20th century. In order to transform the area into an effective base

for 21st century innovation, the KING SKYFRONT project focuses on several key themes: health, medicine, welfare, and environment, as affirmed by Takao Abe, mayor of Kawasaki City. Abe believes that addressing contemporary issues such as the rapidly ageing society and environmental sustainability is not only vital for but will also spur innovation in Japan.

The Kawasaki City project has evolved into an initiative involving the entire Keihin district conducted with Kanagawa Prefecture and Yokohama City. In 2011, the project was designated by the Japanese government as the Keihin-Rinkai Life Innovation Comprehensive Global Strategic Special Zone, and is set to grow rapidly with the help of recently-approved deregulation and tax-relief measures.

Over the years, Kawasaki has fostered diverse techniques and initiatives to promote recycling and alternative energy sources as part of efforts to reduce industrial pollution and harmful impacts on the environment. To advance developments in biomedical and health sciences, many Kawasaki-based chemical and food industries are now notably contributing to these areas. For example, the Nippon Oil and Fats (NOF) Corporation has a research laboratory and industrial plant in Kawasaki, where projects are under way to develop medicines and drug delivery systems. In addition, Ajinomoto — widely known throughout the food industry as the world's most successful manufacturer of amino acids — is expanding its activities into the medical sector, with core research activities, development, and production facilities based in Kawasaki.

Creating an infrastructure for advanced medicine

The Keihin-Rinkai Life Innovation Comprehensive Global Strategic Special Zone focuses on three main areas of advancement in medicine:

regenerative medicine, treatment of cancers and lifestyle diseases, and public health and preventive medicine. To encourage private-sector-driven innovation through industrial clusters within the special zone, three policy points have been established. The first of these involves constructing a database of health information to promote the advancement of personalised and preventive medicine. Development of a sample bank and information network based on Ajinomoto's 'amino index' technology is also being planned.

The second point concerns the promotion of joint global clinical trials and commercial activities aimed at developing Japanese products for the Asian market and overcoming burdensome regulatory and bureaucratic requirements that often delay the advancement of drugs and devices to market in Japan.

The Central Institute for Experimental Animals (CIEA) and the National Institute of Health Sciences (NIHS) will also play a significant role in meeting these goals. The CIEA has been conducting research and development in the inland area of Kawasaki, and in 2011, the institute transferred its base to new facilities at the KING SKYFRONT to step up research, development, and collaborative activities.

The NIHS is making plans to move to KING SKYFRONT from Tokyo. As the oldest national research institute for the testing of pharmaceutical products in Japan, the NIHS has a history of over 130 years of advancing health sciences. The institute currently conducts testing and research for the evaluation of the quality, safety, and efficacy of pharmaceutical products, foods, and chemical substances found in daily life.

As part of the new plans, the NIHS will play a central role in regulatory science activities, establishing methods of evaluation and analysis of new drugs and advanced medical technology, in coordination with international examination bodies. By establishing global standards,



KAWASAKI CITY

significant strides in regenerative medicine for clinical application are expected. In addition, by combining the wealth of resources and know-how of the NIHS and the CIEA, it is intended to make KING SKYFRONT into the hub of a global clinical trial network in Asia.

Due to its proximity to Haneda Airport, KING SKYFRONT will be conveniently accessible to international researchers and businesspersons. Visitors from nearby South Korea and China will have more opportunities to participate in collaborative research and attend day conferences. In addition, in March 2011 the Tokyo International Air Cargo Terminal (TIACT) at Haneda Airport set up a space dedicated to showcasing pharmaceutical products, creating the infrastructure for a logistics hub devoted to the import and export of investigational drugs for clinical trials conducted in Asia.

By establishing a sound knowledge base and attracting top talent to the area, KING SKYFRONT is projected to become a leading centre for global clinical trials, innovative drug development and the advancement of medical equipment and technologies.

A meeting place for seeds and needs

The third policy point concerns the commercialization of advanced fundamental technologies produced by universities and research institutions and expansion of the existing industries in the medical and healthcare sector. As part of these efforts, the tentatively-named Industry-Academia-Government-Citizen Collaborative Research Center is scheduled to be launched at KING SKYFRONT as a leading base for world-class collaborative research. The research centre aims to promote a diverse range of activities through cooperation with leading research bodies. Kawasaki City's Health and Safety Research Center and Environmental Research Institute, will be established on the second and third floors of the centre. The fourth floor will host laboratories for corporations and universities developing leading-edge, advanced technologies. There are plans for both Japanese and

overseas corporations and research institutes to establish facilities at the centre.

In addition, three science parks based in the Kawasaki area will play an important role in nurturing innovation and serving as ideal meeting places for matching seeds from academia with the needs of industry. The first is Kanagawa Science Park (KSP), established in 1989 as the first science park in Japan. Kanagawa Science Park serves as an incubator in collaboration with the Kanagawa Academy of Science and Technology (KAST) to create new research-driven enterprises.

Secondly, the Shin-Kawasaki Forest of Creation is a notable base for industry-academia collaboration established in 2000. In addition to the Shin-Kawasaki Town Campus (K2 Town Campus) that runs research and development programmes in collaboration with Kawasaki City and the Kawasaki Business Incubation Center (KBIC), in September 2012, the Global Nano Micro Technology Business Incubation Center (NANOBI) is scheduled to be completed. The NANOBI facilities will house a large-scale 'clean room' for various operations ranging from processing, trial manufacture, and measurement to evaluation in the nano/micro domain, bringing together the expertise of academia and industry to advance research and development in the very latest nano- and micro-technologies. The clean room will be equipped with cutting-edge equipment from Keio University, Waseda University, Tokyo Institute of Technology, and the University of Tokyo, and will also be available for use by private corporations. At the K2 Town Campus, research will encompass not only medical and engineering fields but also programmes to advance electric vehicle development and other new industry creation projects, with the help of some of the latest developments in the world's fastest optical fiber networks.

The third science park is the Techno Hub Innovation Kawasaki (THINK) developed by one of Japan's largest steel producers, the JFE Group. The science park is capable of accommodating

large-scale projects and wet-lab experiments; the wet laboratory is one of the core facilities of the Entrepreneur Asian Village operated by Kawasaki City.

It is widely anticipated that focusing on high value added production will bring nanotechnology into the mainstream of manufacturing technology, and lead to greater output of environmental and biotechnological products. In the domain of biotechnology, KING SKYFRONT will enable researchers to carry out wet-lab investigations, that are currently not possible at the Shin-Kawasaki Forest of Creation and the KSP. Both the National Institute of Health Sciences and the Industry-Academia-Government-Citizen Collaborative Research Center will be capable of accommodating Biosafety Level 3 research, meaning that at least two Biosafety Level 3 laboratories will become available within the next few years. Additionally, the Urban Renaissance Agency in its role as landowner is promoting the establishment of new business facilities to encourage global corporations to set up research and business bases to spur innovation under private-sector initiatives.

With environmental and sustainability issues and principles firmly in mind, KING SKYFRONT is an audacious, large-scale feat of strength in combining Kawasaki's impressive manufacturing history and new efforts to stimulate economic growth of the region's life sciences sector. Through innovative land development, Kawasaki aims to continue raising the bar in high-value-added manufacturing and to drive research, development and commercialisation at both the national and international level.

City of Kawasaki

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For further information about establishing your business at KING SKYFRONT:
Urban Renaissance Agency

www.ur-net.go.jp/sitemap/english.html
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KAWASAKI KING SKYFRONT PROJECT

1



Hideyuki Okano

Professor, Department of Physiology, Keio University School of Medicine
Chair, Graduate School of Medicine, Keio University

Accelerating the realization of regenerative medicine

Diverse and multi-tier collaborations by the Central Institute for Experimental Animals at the KING SKYFRONT are paving the way to clinical applications as a foundation for the development of regenerative medicine.

An eminent world expert in the field of molecular neurobiology, developmental biology, and tissue engineering, Professor Hideyuki Okano from the Department of Physiology at the Keio University School of Medicine is a leading figure in collaborative research with the Central Institute for Experimental Animals (CIEA) and has been involved with CIEA projects for more than ten years.

Okano and his colleagues are renowned for developing the world's first spinal cord injury model of a marmoset—a type of primate—in 2005, and for successfully transplanting neural stem cells derived from a human foetus into a marmoset. Okano also used hepatocyte growth factor (HGF) in a preclinical study of the spinal cord injury model, which led to a clinical trial of amyotrophic lateral sclerosis (ALS).

Okano's next goal is to establish a model for spinal cord injury treatment using iPS cells (Induced pluripotent stem cells). "We have already transplanted neural stem cells produced from iPS cells into the spinal cord injury model of a marmoset and succeeded in the restoration of motor functions,"

explains Okano. "In order to translate these results into clinical applications, we must delve further into the functional recovery mechanism, immunological rejection, and the image analysis of transplanted cells, and it is regarding these points that a collaborative project with the CIEA becomes increasingly important."

Preclinical study transforming into clinical practice

Mice are the traditional choice of experimental animal used in translational research. However, going against the norm, Okano introduced to his research the use of severe immunodeficient mice (NOG mice), which were developed by the CIEA. "The use of NOG mice allows us to more precisely follow the behaviour of human stem cells, cells derived from stem cells, and cancer cells," says Okano.

After the development of the marmoset spinal cord injury model in 2005, Okano went on to collaborate with the CIEA to produce the world's first transgenic marmosets (Sasaki, E. *et al. Nature* **459**, 523-527(2009)). "It is the first time we have used primates to



analyze the germ line transmission of the transgene," says Okano. "By using this approach, we are now making various model animals for the treatment of neuropsychiatric disorders, such as Alzheimer's disease and autism. I believe these animals will become excellent models for new drug development, and will also assist in the clarification of various pathological conditions."

Preemptive medicine

The most common type of dementia affecting more than 26 million people worldwide, Alzheimer's disease is a major public health concern in aging societies such as Japan. Alzheimer's disease takes a long time to develop, and Okano explains it is therefore of major significance to conduct experiments on long-lived marmosets. "With the model of Alzheimer's for transgenic marmosets, we can use MRI and PET to observe the types of changes that will occur in the course of development over the long term. In this way, we can predict how many years it will take for the disease to develop."

Okano emphasizes the importance of preemptive medicine for the future. "Eventually, it might become possible to prevent the disorder

if we use iPS cells or marmosets for analysis. To do this, multiomics, as well as systems biology and systems medicine, are needed to comprehensively process life information at different hierarchy levels. In collaboration with various departments at Keio University, we want to understand the pathological condition to further expand upon integrated information, but the outcome is limited for a single university."

Here Okano highlights the significance of collaboration. "We work together with the National Institute of Health Sciences to develop the official assay system of new drugs, and we work closely with the CIEA to analyze the pathological condition of the *in vivo* experimental approach using primates. Our bodies consist of DNA, cells, tissues, and individual organisms. Collaboration with research facilities holding a wealth of specialties is important to connect each hierarchy. KING SKYFRONT holds great potential to become a leading venue for collaborative research in regenerative medicine, drug development and therapeutic treatments."

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KAWASAKI KING SKYFRONT PROJECT

2



Ryuta Nomura

Executive Director
Central Institute for Experimental Animals

Edging closer towards personalised medicine

As a prominent new life science and innovation centre at KING SKYFRONT, the Central Institute for Experimental Animals will provide a strong foundation for advancing biomedicine, with future collaborations planned with the National Institute of Health Sciences.

The Central Institute for Experimental Animals (CIEA), with its new operational facilities located at KING SKYFRONT in Kawasaki, is a leading centre for basic research in medical sciences and translational research, from laboratory to clinical practice. The CIEA is primarily engaged in *in vivo* studies using animal models to advance experimental medicine. The founding director and chairman of CIEA, Tatsuji Nomura, began his career as a researcher in basic medicine and later established the CIEA to build on Japan's infrastructure for biomedical research.

"During the first 40 years, we developed a technique to produce standardised groups of experimental animals," says Ryuta Nomura, the CIEA's executive director, and son of the founding director. "Building on this foundation, we have been able to develop some of the most advanced experimental animal models over the last 20 years."

World-class experimental animal models

The cutting edge experimental models created by scientists at the CIEA include the polio mouse,

rash2 mouse, NOG mouse, and genetically modified marmosets. The polio mouse was developed for assessing neurovirulence of the live polio vaccine and is currently used as an official animal-assay in the Global Polio Eradication Initiative led by the World Health Organization (WHO). The rash2 mouse was developed to evaluate short-term carcinogenicity and has reduced the duration of carcinogenicity testing from two years to six months, a notable advancement for drug development. CIEA'S achievements have received considerable acclaim from world regulatory agencies, particularly the FDA; US, EU and Japanese governments had invested more than 10 years conducting developmental work towards the practical application of the rash2 mouse.

The NOG mouse is a new generation of severely immunodeficient mouse that can be used to develop a wide variety of humanized mice. "The introduction of human haematopoietic stem cells (HSCs) helped produce a mouse replaced with nearly 70% humanized



blood," explains Nomura. "There is also a mouse with a humanized liver with nearly 80% replacement that can be used to study the metabolic dynamics of pharmaceutical products. In the early 1960s, the side-effects of thalidomide became a worldwide problem. These harmful effects might well have been avoided if the NOG mouse with humanized liver were available at the time." Research at the CIEA is not limited to mice. Erika Sasaki and co-workers at the CIEA have successfully developed the world's first genetically modified transgenic primate, the transgenic marmoset, in collaboration with Hideyuki Okano of the Keio University School of Medicine.

The bold promises of regenerative medicine

The overarching goal of the CIEA at KING SKYFRONT is to develop accepted standards for safety in the development of new drugs and advanced medical technology. "In the future, we are going to work with the National Institute of Health Sciences (NIHS) to develop standard approaches for safety in assessing substrates for regenerative medicine," Nomura says. "To this end, the CIEA will play a significant role in *in vivo* research."

Another longstanding goal is the realisation of personalised medicine. By transplanting human cancer cells into NOG mice to reproduce the same tissue inside

the mouse body, a Viable Cancer Xenograft (VCZ) model can be constructed to enable observation and analysis of live cancer cells. The next step will be to achieve the ultimate goal of personalised medicine. "If I get cancer, we can create a NOG mouse by injecting my cancer cells into the mouse," says Nomura. "We can use the mouse to test which medicine works best for me and decide on the course of treatment. By updating common practices so that experimental animal models can be used for the development of pharmaceutical products and for safety studies that will aid healthcare professionals at hospitals, I believe we can make further contributions in the medical humanities."

Gazing across the Tama River at Haneda Airport, on the opposite shore of the CIEA, Nomura concludes, "My aim is to make the CIEA a prime venue for Asia-wide collaborative studies along with Singapore, China, and South Korea, and at the same time, to encourage international corporations and research institutes to conduct collaborative experiments on a global scale. The door to our collaborative research facilities is always open."

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Commitment to excellence in amino acid science and healthcare

As the world's biggest manufacturer and supplier of amino acids, backed by formidable capabilities in amino acid analysis technologies, Ajinomoto has successfully developed the world's first method for conducting health checks using amino acids called AminoIndex™ — a novel screening marker already being used to evaluate cancer probability and set to be expanded into applications for a variety of other medical conditions.

Ajinomoto is renowned as a global manufacturer of seasonings, processed foods, amino acids, pharmaceuticals and specialty chemicals. With worldwide business locations in 26 countries, Ajinomoto is actively contributing to the advancement of food and human health sciences, underscored by its extensive knowledge, expertise and application of amino acid technologies.

The history of the company is closely intertwined with developments in amino acid science. Yutaka Kunimoto, Ajinomoto's corporate executive deputy president, explains, "Professor Kikunae Ikeda at the then Tokyo Imperial University, the former of Tokyo University found that stock made from simmered kelp contains an ingredient with a flavour that cannot be explained by the four previously known basic taste modalities — sweet, salty, sour and bitter. After extensive research, he identified the ingredient as glutamic acid, an amino acid, and named its flavour umami. Later, he approached the industrialist Saburotsuke Suzuki, and in 1909, Suzuki commercialised monosodium glutamate to start marketing the product known as Ajinomoto® around the world. That was the beginning of our company."

Ajinomoto's Kawasaki Works, comprising a large network of research institutes, is located in Suzuki-cho, named after the corporate

founder Saburotsuke Suzuki II. It was at this site that Ajinomoto constructed the Kawasaki Plant in 1914.

More than 100 years since its foundation, Ajinomoto continues to contribute to major advancements in amino acid science — its scope of research has expanded from glutamic acid to a wide range of other amino acids, as well as nutrition and human health. Over the years, Ajinomoto has become the number-one manufacturer and supplier of amino acids and has gained a considerable advantage in the development of amino acid analysis technologies. The company's product line-up has expanded from seasonings and processed foods to specialty chemicals, health foods and precision equipment materials. Ajinomoto is also focusing on various applications in the field of medicine, with the latest example of its successes being the development of AminoIndex™.

Amino acids and health science

Kazuya Onomichi, who heads Ajinomoto's Frontier Research Labs, comments, "More than 40 types of amino acids are known to exist in human blood. Normally, the concentration of each amino acid is maintained via the body's homeostatic functions. However, any disruptions in terms of nutrition or onset of disease can cause an imbalance in blood amino acid concentrations, partly due to changes in metabolic functions."

It has been shown that many diseases are closely related to amino-acid imbalances. "Using conventional methods, it is often difficult to evaluate the nutritional status and to determine the onset and progression of disease by checking the balance of blood amino acid concentrations," says Onomichi. "However, by making continual advancements in our amino acid research, we have been able to develop



Kazuya Onomichi, head of Ajinomoto's Frontier Research Labs.

amino acid analysis technologies that can be readily adopted at medical facilities. That is the basis of our AminoIndex technology."

The proprietary AminoIndex technology developed by Ajinomoto is designed to assess the risk of disease onset by comparing certain indices between the subject and those diagnosed with various diseases. These indices are developed by measuring the concentrations of multiple amino acids in the blood. The technology relies on a multivariate analysis based on bioinformatics and studying correlations between amino acids.

"The world's first automatic amino acid analyser was developed in the 1950s," says Onomichi. "The first analyser was installed by the US pharmaceutical and chemical company Merck, and the second one by Ajinomoto." By continually furthering amino acid research, Ajinomoto has built a large-scale R&D platform capable of leading to various applications. Examples include infusions containing amino acids as central ingredients and a branched-chain amino acid preparation named 'Livact' for liver diseases. Today, research into pharmaceutical and health applications forms an important part of Ajinomoto's business operations.

There are thought to be two main reasons behind Ajinomoto's successful commercialisation of the AminoIndex technology, in addition



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to its fundamental expertise in amino acid analysis technology. First, collaboration with other companies to develop reagents and instruments that allow for high-throughput analysis of amino acids in the blood is a significant factor. These types of analyses typically used to require at least two hours using conventional instruments. Now, new equipment enables analysis to be completed within just seven minutes. Secondly, at room temperature, blood samples can have different amino acid concentrations at the sampling stage and analysis stage; this problem can be circumvented using a new refrigerated transporter named Cube Cooler® (SuperCooler), jointly developed by Ajinomoto and partner companies, to create an environment that prevents blood samples from deteriorating.

"The amino acid balance is known to deteriorate in many types of disease, including cancer, atherosclerosis and other cardiovascular diseases, lifestyle-related diseases and Alzheimer's disease," says Onomichi. "AminoIndex™ has been commercialised for cancer screening. We hope that more and more patients undergo these types of screenings, and we aim to contribute to the health and wellbeing of a greater number of people. We plan to develop applications of this technology to other diseases."

Screening for many forms of cancer

In April 2011, the AminoIndex™ Cancer Screening (AICS) was commercialised for the risk screening of stomach cancer, lung cancer, colorectal cancer, prostate cancer and breast cancer. In addition, in May 2012, the technology was developed for the screening of gynaecological cancers, including cervical cancer, endometrial cancer and ovarian cancer.

Ryota Yoshimoto, general manager of the AminoIndex Department, notes that the high cancer mortality rate in Japan was the

compelling reason behind the selection of cancer as the focus of application of the technology.

As of June 2012, the AICS technique is performed at around 300 medical check-up facilities and other medical facilities throughout Japan. Blood samples are sent to an external institution for analysis of amino acids, and the results are then sent to Ajinomoto for further analysis. The medical facility informs those who undergo screening about the AICS results within one to two weeks. The individual can obtain information about the risks of falling in four types of cancer in men and five types in women with a single blood sample. The level of risk is graded on a scale from A to C.

"We can identify the type of cancer using a single test, as the blood amino acid concentration varies according to cancer types," says Yoshimoto. "And as clinical trials have progressed, we have also discovered that the test is almost equally sensitive to early-stage and advanced cancer."

Yoshimoto continues to explain some of the implications of AICS for company-wide medical check-ups and health screening programmes: "Today in Japan, the proportion of people undergoing cancer screening is not large enough. In many cases, fear of pain, discomfort and other forms of psychological resistance to tests may act as barriers to taking conventional screening tests. With AICS, however, the screening can be conducted using blood sampling alone. As blood samples are usually taken during routine health check-ups, the process can be greatly simplified for both the individual undergoing the test and medical personnel. We are hoping that more widespread use of AICS will lift the rate of participation in screening tests during medical check-ups and increase the frequency of early detection."

Yoshimoto notes that his team is looking at ways of increasing the number of applicable

cancer types for AICS and expanding its scope to other diseases: "We are now conducting clinical trials of the technology on pancreatic cancer. We also hope that the AminoIndex technology will contribute towards more accurate diagnosis in connection with the risk of developing lifestyle-related diseases, and with metabolic syndrome, which is currently diagnosed on the basis of waist circumference and body mass index."

Contributing to detection of cancerous and precancerous states

One of the first hospitals to introduce AICS was the Centre for Multiphasic Health Testing and Services of Mitsui Memorial Hospital in Tokyo. In September 2011, AICS was added as an optional test in the health screening programme at the centre. "We encountered the AminoIndex technology during the course of our constant search for technologies that help us predict and prevent diseases," says Minoru Yamakado, director of the centre.

Many people currently visit the hospital specifically for the AICS testing, with some even journeying from far away regions of Japan. "Even visitors who don't know about AICS often decide to add this option when we provide the information. Despite the cost, people appreciate the ease of testing, which requires only five millilitres of blood," says Yamakado.

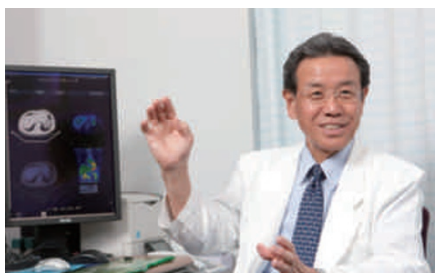
The number of people requesting AICS has been steadily increasing. By the end of March 2012, nearly 300 people had undergone AICS testing at the centre.

Yamakado explains, "29 out of 257 test subjects were rated in the Rank C category, a group of people with a high risk of lung cancer. Of these subjects, 21 completed a computed tomography (CT) scan. One of them was suspected of having lung cancer, and some form of precancerous state was detected in 13 people



Courtesy of Kawasaki City

Eat Well, Live Well.
AJINOMOTO.



Minoru Yamakado is director of the Centre for Multiphasic Health Testing and Services at Mitsui Memorial Hospital, Tokyo.

including this individual. As for stomach cancer, 16 out of 257 test subjects were rated in the Rank C category, and eight out of 12 people were diagnosed with atrophic gastritis, which has a risk of advancing to cancer in the future if unattended. Undoubtedly, we could at least detect many precancerous states."

Yamakado adds: "As our AICS-led achievements accumulate, imaging techniques such as CT and positron emission topography (PET) may become unnecessary for cancer screening. Instead, a combination of AICS and ultrasound diagnosis may become the leading choice for health screening programmes."

To bring these ideas to fruition, Yamakado is aware of the need for AICS to expand its scope to other cancer types. "It is particularly difficult to detect pancreatic cancer, even with ultrasound," he says. "Hopefully, some day in near future, AICS will become the predominant method of detecting cancer."

Towards a global standard

In recognition of the unique technology borne out of research conducted in Kawasaki, the City of Kawasaki itself has high hopes for the AminoIndex technology. "It is our sincere hope that the technology will become the global standard," says Nobuhide Kobayashi,

executive director of Kawasaki City's Coastal Area International Strategy Office.

Japan's ageing population and decline in birthrate are seen as critical issues by health care professionals around the world. The Keihin-Rinkai Life Innovation Comprehensive Global Strategic Special Zone, promoted by the City of Kawasaki in collaboration with Ajinomoto and many other companies, is being transformed into a hub for life sciences and innovation in Japan, with the potential to become a leading centre in terms of human health.

"Instead of presenting a single, universal method, the AminoIndex technology will probably be localised in each country, in a similar way in which Ajinomoto has introduced various food products appropriate to the culture of each country," Kobayashi explains.

Kobayashi envisions that such an approach will help to transform the image of Kawasaki. "Today, few people are yet aware of Kawasaki as a hub for life science innovation, associating the area primarily with the chemical and heavy industries that supported Japan during its years of spectacular economic growth. However, with the rise of AminoIndex technology on a global scale, the image of Kawasaki may change."

Kunimoto expresses his hope that "Ajinomoto will be recognised around the world as a company making contributions to food, life science and health using of the world's number-one amino acid technologies." To this end, Ajinomoto will be actively forming extensive partnerships both in Japan and abroad.

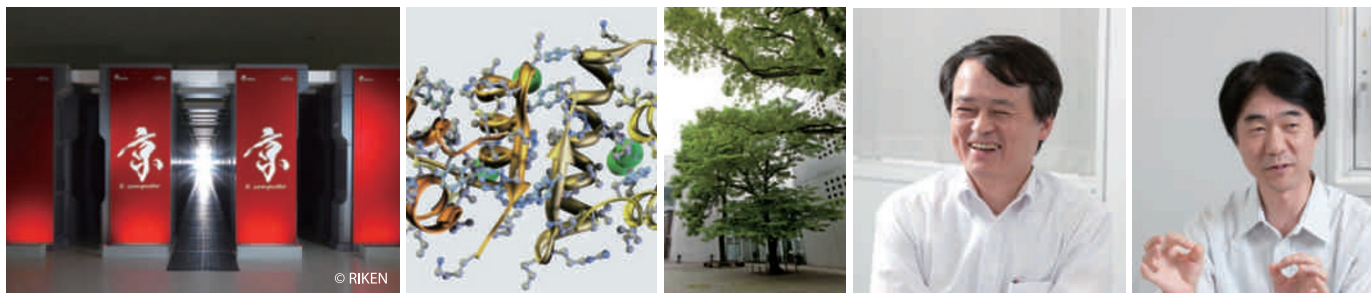
"AminoIndex technology may one day help to achieve the goal of personalised medicine and preventive medicine. However, this dream will not be realised through one particular technology or one particular company alone. The Keihin-Rinkai Zone will closely monitor how the AminoIndex technology functions within and contributes to the entire system.

While looking at this process, we will consider collaboration with other parties that may have different strengths," Kunimoto adds.

Today, Ajinomoto's annual R&D budget totals approximately 38 billion yen. Comprising a workforce of around 4,000, with 1,300 engaged in research and development, Ajinomoto's R&D capability accounts for a notably high percentage for a food company in Japan. Ajinomoto is consistently ranked as being among the top companies in the food and beverage and tobacco-related sector by The Patent Board, a leading provider of best practices research, based on comprehensive evaluation of registered patents and cited patents in the United States.

Ajinomoto, with its roots in amino acid science more than a century ago, is about to embark on a new health revolution based on the remarkable utility of amino acids. On whether Ajinomoto had anticipated the potential of amino acid science to achieve its prominence as a company with vast research and development resources, Kunimoto comments: "I am not sure whether we had anticipated the potential, or if we discovered the potential during the process of our R&D efforts. One thing is certain: We are a unique food company persistently striving to develop advanced technologies based on unique substances called amino acids, located at the nexus of food science, nutrition, and human health. Our unceasing efforts to make significant advancements based on amino acid science is driven by a vision of creating new values and fostering a pioneer spirit."

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FUJITSU LIMITED

Supercomputing for drug discovery

Fujitsu is making waves with a project that aims to develop new drugs to target cancer and a host of other diseases through strategic collaborations with the University of Tokyo, pharmaceutical companies, and a government agency in Singapore.

By utilising some of the very latest high-speed supercomputing technologies, drug discovery and development is set to be revolutionised.

More than a quarter of a century ago, Fujitsu began to explore the possibilities of applying computer technologies to the field of drug design and development. Masahito Yamaguchi, Vice President of Bio-IT Development Office comments, "Initially, simulation software came from abroad — and later, when Fujitsu developed its own software, it became possible for us to achieve great accuracy." In a significant step forward, a new drug developed as a result of some of the latest simulations and research conducted jointly with the Research Center for Advanced Science and Technology and three pharmaceutical companies is scheduled to be revealed in the fall of 2012.

"Fujitsu has two roles in this new drug development project," explains Shunji Matsumoto, Senior Director of the Bio-IT Development Office. "The first is to discover a low-molecular weight compound that works as a drug to target proteins that cause disorders. The second is to simulate the binding energy of the drug-protein complex with a high degree of accuracy in order to assess the likely efficacy of the drug." In order to identify candidate drugs, Fujitsu developed an application called Optimum Packing of Molecular Fragments (OPMF), and for evaluation of drug efficacy, Fujitsu has developed a binding affinity prediction system — MAssivelyParallel Computation

of Absolute binding Free Energy with well-Equilibrated system (MAPLE CAFE) — which as of 2005 "delivers the highest accuracy in the world" according to Matsumoto.

One of the main characteristics of MAPLE CAFE is its capacity to run simulations simultaneously in a massively parallel environment. Running 400 Central Processing Units (CPUs) simultaneously, the system enables calculations that would ordinarily take 30 years using one CPU to be completed in a single week. The speed of the simulations, however, remains a challenge as it can take up to several months to assess the effectiveness of a candidate drug.

The rise of the supercomputer has now dramatically increased processing speeds for drug discovery and development. As of the summer of 2012, Fujitsu has been refocusing its activities in this area, with plans to hand over the latter stages of drug synthesis to pharmaceutical companies. One high-profile example is the globally-renowned K Computer located at the RIKEN facility on Port Island, Kobe. The supercomputer, certified as the world's fastest in the LINPACK Benchmark in June and November 2011 was jointly designed and developed by RIKEN and employees from Fujitsu's Kawasaki factory. "With the development of the K Computer, it takes only a week to perform 2,000 simulations," says Matsumoto.

Since March 2012, Fujitsu's commercial supercomputer system, equipped with an Intel CPU, has been running simulations required for the drug discovery project for the treatment of cancer and lifestyle related diseases.

As of September 2012, the K computer is scheduled to perform these simulations — a radical development that is expected to slash the computation time to approximately one-tenth. Another factor is the optimization for

the K computer of GROningen MACHine for Chemical Simulations (GROMACS) — a free package for molecular dynamic simulations which was originally designed to run optimally with Intel CPUs - currently being carried out at Stockholm University. Optimization of GROMACS for the K Computer is expected to accelerate the speed of drug development.

"Conducting fast molecular computations opens up the possibility of creating new drugs that may previously have been impossible to develop," says Matsumoto. "The latest technologies enable us to confirm whether the molecules interact with other proteins, meaning that we can determine the risk of adverse effects and ultimately reduce the time and costs involved in drug trials following the drug design process."

Fujitsu is also engaged in conducting so-called 'IT drug discovery' projects together with Singapore's lead government agency dedicated to fostering world-class scientific research, the Agency for Science, Technology and Research (A*STAR), with the goal of developing novel drugs for cancer treatment, as well as for infectious diseases such as Japanese encephalitis and West Nile fever.

Considering the advantages of collaborative research undertaken with other industrial, academic and governmental bodies, Yamaguchi comments, "The major benefit is being able to examine the work from different perspectives, which is something that cannot be achieved by us alone. Our aim is to increase the speed of analysis even further; this will ultimately enable us to focus on new software development and its applications."

FUJITSU LIMITED
www.fujitsu.com

*The K computer is a registered trademark of the RIKEN Advanced Science Institute.



NIPPON MEDICAL SCHOOL, MUSASHIKOSUGI HOSPITAL



A collaborative approach to community healthcare

For over 75 years, Nippon Medical School's Musashikosugi Hospital located in Nakahara Ward, Kawasaki has played a crucial role in community healthcare, promoting collaboration among departments so that patients receive the best and most advanced medical care.

Established in 1937, Musashikosugi Hospital, formerly known as Maruko Hospital, is one of Nippon Medical School's four major hospitals in the Kawasaki region. The hospital has 372 beds and a total of 32 departments and provides a wide range of high-quality healthcare services to community residents

"In a general hospital, it is important for all departments to work together smoothly," says Akira Kurokawa, director of Musashikosugi Hospital. "Without doing so, we would not be fully utilising the hospital's collective strengths." In order to focus on strengthening interdepartmental partnerships at the hospital, considerable efforts have been made in the past few years.

"We opened a centre to act as a bridge between related departments. If the different departments are the 'warp' of the hospital, then this centre is the 'weft'. By integrating our activities in this way, the hospital has become better able to serve and contribute to the community," says Kurokawa.

Notably, the hospital's Department of Critical Care Medicine established in 2003 was designated by the Japanese government as a Critical Care Medical and Surgical Center in 2006. Kurokawa is a strong advocate of critical care, having been one of the original staff members of the Critical Care Medical and Surgical Center of Nippon Medical School Hospital in Bunkyo Ward, Tokyo — the first of its kind in Japan.

"We currently have six doctors and three interns treating emergency patients, who may require specialised treatments that span several

departments," says Kiyoshi Matsuda, a professor at Musashikosugi Hospital's Department of Critical Care Medicine. Supported by the expertise of neurosurgeons, orthopaedic surgeons, and general surgeons, the centre provides various types and levels of intensive care.

Matsuda is an expert in critical care with 28 years' experience, and arrived at the hospital in April 2012. He comments that reducing the time to treatment is one of the main challenges to overcome: "In particular, we recognised the need to prepare our own emergency response vehicles, without reliance on external doctors and nurses, so that patients could be smoothly transferred from other hospitals."



Akira Kurokawa, director of Nippon Medical School's Musashikosugi Hospital.

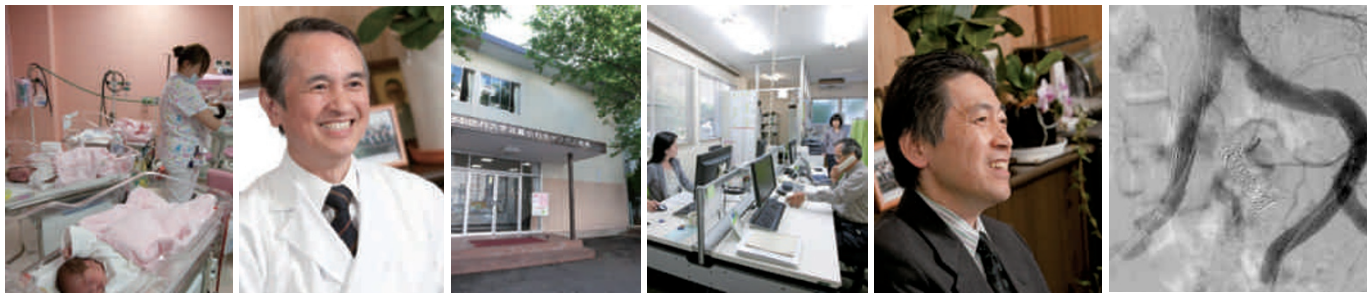
As a result, in June 2012, Musashikosugi Hospital began operating an emergency response vehicle staffed by its own medical personnel. Matsuda also notes the importance of Musashikosugi Hospital's standing as a university hospital. "Not all of the trainees working here will necessarily become emergency physicians in the future. However, it is likely that they will need to be prepared for emergency situations, regardless of the department to which they may be assigned," he says. "As a training facility, we have many opportunities to treat patients transferred to the centre. Trainees can learn the basics of emergency treatment based on these

experiences. I hope many of them will go on to become physicians who can contribute to emergency medical care both in the community and nationwide in their future careers."

Improving neonatal and pediatric care

Nakahara Ward, one of seven in the Kawasaki region, has the greatest number of residents but the lowest average age. "Amongst Japan's ageing population, it is unusual to see a regional increase in the number of children aged 14 or younger during the past twenty years," says Yasuhiro Katsube, assistant professor at Nippon Medical School's Department of Pediatrics. With this growth in the young population, the Kawasaki region has seen a higher demand for specialists in obstetrics and pediatrics. The Newborn and Infant Medical Center began full-scale operations in October 2011 providing obstetric care and treatments related to neonatal medicine and pediatrics. The bed capacity at the Neonatal Intensive Care Unit (NICU) has increased from three to six, and the Growing Care Unit (GCU) from six to twelve. Doctors and nurses who have trained at other neonatal intensive care units play a central role at the Newborn and Infant Medical Center.

"We estimated that a total of 30 beds would be needed at the NICU in Kawasaki," says Katsube. "However, the shortage of beds continued, resulting in an outflow of patients to neighboring Tokyo and Yokohama. After the expansion at the hospital, we have been able to make a greater contribution than before, even with the shortage of beds. With the addition of pediatric surgery, we understand the significance of our contribution through our conversations with practitioners in the community. We are now able to treat patients, for example, with high-risk pregnancies and children with serious illnesses, which presents new challenges for our medical staff."



The Department of Pediatrics today provides comprehensive diagnosis and treatment for a wide range of cases. Each physician coordinates closely with a number of other departments at the hospital to treat conditions requiring particular expertise.

Leading the fight against dementia

Musashikosugi Hospital is also actively involved in geriatric care. The Dementia Consultation Center was established in 2007 and ran until 2012 as part of the Academic Frontier Project for Private Universities supported by the Japanese government. Although the project has now concluded the centre remains very much committed to fighting against dementia.

"Both medical care and nursing care are important for dementia patients," says Shin Kitamura, a professor at Musashikosugi Hospital's Department of Internal Medicine. "We must make community-wide efforts to support those with dementia." In the past, the number of facilities where people could seek sound advice and information about dementia was limited.

"The government plans to establish 150 medical centres for dementia care across the country, and to have counselling centres located inside hospitals. In consideration of the distress that may be experienced by those visiting consultation centres, we have opened a counseling centre outside the hospital that offers free counselling services."

As of April 2012, a total of 3,185 people have visited the centre for counselling. Whilst family members can come to the centre for consultations, patients can also attend in person. In this case the patient is asked to undergo preliminary screening by completing a cognitive test administered via a touch screen panel and rated on scale of one to fifteen. If the patient's score is below twelve, a more detailed examination and interview are scheduled. The results of the test are summarised in a referral letter addressed to the client's primary physician. So far, the centre

has issued a total of 978 referral letters.

Kitamura says, "Without the resources of the counselling centre, those 978 people would not have had the opportunity to discuss their dementia diagnosis with their primary doctors. We are proud that we can contribute to early detection in this way." The number of people visiting the counseling centre has been increasing; twenty to thirty new visitors now seek information at the centre each month. The centre is also supported by a team of community volunteers.

"I hope that more people have an understanding of dementia, so that we can better identify the symptoms and provide treatments at an early stage," says Kitamura.

Building on tradition to advance medical treatment

Musashikosugi Hospital has recently opened a new centre called the Interventional Radiology and Minimally Invasive Care Center. The head of the centre, Hiroyuki Tajima, comments, "The reason why the name of our centre includes the term 'minimally invasive' is that we wanted to emphasise our expertise in these cutting edge techniques."

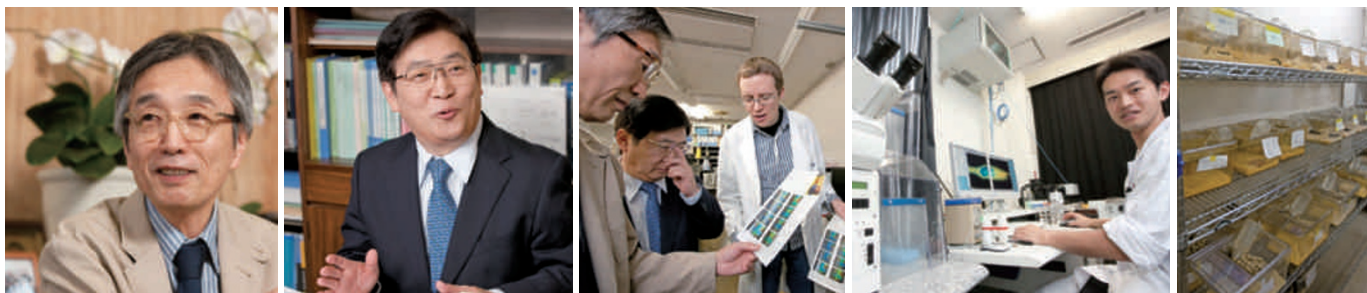
With the latest advancements in medicine, treatments can be administered and guided by a monitor using catheter-based techniques, circumventing the need for highly invasive surgeries such as craniotomies, thoracotomies, and laparotomies. The minimally invasive approach reduces the need for hospitalisation, and patients tend to recover much faster, returning to daily life smoothly after surgery. There has been an increasing demand for minimally invasive haemostatic techniques for injuries involving major bleeding; for example, a medical agent called Histoacryl can be introduced through a catheter to restrain haemorrhaging from the blood vessels. This particular procedure requires specialised techniques due to the recent rise in the number of patients

taking medication to thin the blood for the prevention of cerebral infarction and other disorders. Musashikosugi Hospital has three full-time physicians who are capable of performing this procedure. Currently, this treatment is not covered by insurance and has been the subject of discussions conducted by in-house ethics committees. Tajima asserts that the hospital's proactive stance in providing highly advanced medical treatment is a 'hallmark tradition' of Nippon Medical School.

In addition, Kurokawa emphasises the importance of embracing progressive approaches to advance research at university hospitals. "We strive to be ahead of the times in realising cutting-edge medical practices, and in strengthening our collaborative partnerships by opening additional facilities. We plan to open a cancer treatment centre in the near future. In doing so, we can nurture an environment where physicians from different departments and paramedics can hold free discussions and ultimately offer better medical care to patients, which is my greatest wish."

Musashikosugi Hospital currently has plans for the construction of a new hospital on adjoining land in 2014. Kurokawa envisions a bright future for the hospital: "We are planning a new building that will accommodate office space for companies engaged in medical care, nursing care and welfare services on the lower floors, care homes and day nurseries on the middle floors, and to create residential space on the upper floors. We believe this will transform Musashikosugi campus into a leading hub for medical care, welfare, and academic research, as part of the goals set out by the Kawasaki City Urban Improvement Bureau, resulting in a major contribution to the wider community."

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INSTITUTE OF DEVELOPMENT AND AGING SCIENCES, NIPPON MEDICAL SCHOOL

Exploring the life and aging sciences



The Institute of Development and Aging Sciences at the Nippon Medical School is the first research institute in Japan to focus on aging sciences. With nearly 60 years of history, this institute continues to research life science issues with a focus on aging much more extensively than before. It works in full coordination with the nearby Nippon Medical School Musashikosugi Hospital in an effort to translate new research findings into clinical practice at the earliest opportunity.

The roots of the Institute of Development and Aging Sciences at Nippon Medical School currently located in Musashikosugi go back to 1954 with the establishment in Tokyo's Chiyoda Ward of its precursor, the Institute of Gerontology, Japan's first research institute for aging. Following its inauguration, the then director, the late Dr. Tomosaburo Ogata carried out research in the role of salivary gland hormones and vitamin E in aging and geriatric diseases and actively participated in conference presentations and submitted research papers. Subsequently, Ogata, through his connection to the Nippon Medical School as a former professor and the institute's association with a number of the university's professors and officials, was instrumental in facilitating the transfer of the institute to the Nippon Medical School in 1968. The institute was later relocated to Bunkyo Ward, Tokyo, and in 1990 moved again to its current location in Musashikosugi.

"Under the same name, the institute has become an organization extensively targeting life science studies, including but not limited to aging sciences, and tests the research results for clinical deployment," explains Shiro Minami, the current director of the institute.

In addition, the institute is responsible for the graduate school program of Nippon

Medical School (Doctor of Medicine) and provides opportunities to study genome science, post-genome science, molecular morphology, and mitochondrial science, neuroendocrinology, and life information sciences. One of the most recent studies advanced by the institute which has drawn the most attention as a unique approach is the application of hydrogen to medical care.

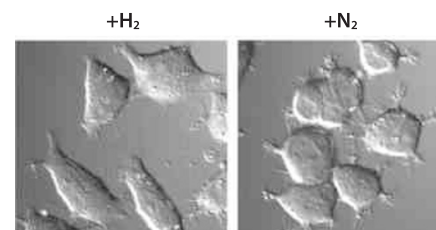
Hydrogen: The smallest of molecules has big potential in anti-aging applications

"Mitochondria are subcellular organelles known to provide energy for cells. However, the reactive oxygen species that is produced in union with oxygen by certain electrons as a by-product is a cause of lifestyle-related diseases and the aging process," explains Shigeo Ohta, a leading expert in mitochondria studies in Japan.

Scientists have extensively explored the deactivation of reactive oxygen species as a solution to the problem; however questions remain as to the most suitable method for deactivation and whether the level of inactivation was too small or great. Ohta focussed on the use of hydrogen gas as an antioxidative substance as a reductant for reactive oxygen species such as hydroxyl radicals, which is the most potent reactive oxygen species encountered in living systems

"I focussed on hydrogen as a deactivating species for reactive oxygen species due to long years of experience as a researcher" says Ohta. "We first experimented with using hydrogen in this role in January 2005 and were astonished when we saw our results. The cells that had been weakened and curled up by exposure to reactive oxygen species were rejuvenated and restored to their original shape when treated with hydrogen and at that point we thought we might be onto something."

Hydrogen has two important physiological



+H₂ contains cells with hydrogen in culture medium. **+N₂** contains cells with nitrogen instead of hydrogen in culture medium, called PC12, and the generation of reactive oxygen species.

characteristics: the rapid circulation within the body due to the small size of the molecules, and the property that combines water solubility and lipid solubility. While other antioxidants circulate through the body via the bloodstream, hydrogen efficiently spreads around the body via diffusion.

"Because the outer part of the cell is lipid and the inner part is water it is easier to handle hydrogen that is oil and water soluble," says Ohta.

The first paper about this study was featured in *Nature Medicine* (June 2007). Since then, five years have passed, and now Ohta and his team are almost ready to obtain results from clinical testing. Despite their favourable progress, Ohta explains the road to success was not a smooth one.

"People did not necessarily have a positive image of hydrogen because there were many products around, such as "hydrogen" water that did not contain any hydrogen. Also, since hydrogen is an all-too-common molecule, some people cannot believe the results."

That alone explains why studies into hydrogen and its potential in the research of anti-aging effects were not extensively pursued until Ohta adopted a serious stance on hydrogen research.

"If I was not doing this research at Nippon Medical School, I would not have been able to start fully-fledged research into hydrogen. Nippon Medical School traditionally places importance on originality and I would not have been able to come this far without the positive environment here."



Reducing side effects through a genomic approach

Minami's ongoing study focuses on genes that contribute to the creation of medication without side effects.

"Any drugs cause side effects, such as rashes and fever, and some strong medicines work to dissolve muscle or annihilate white blood cells," explains Minami. "For anti-cancer agents in particular, the situation is far more serious, and eight out of ten cancer patients suffer from serious side effects. In contrast, some people do not experience any side effects when the same medicine is administered. It is simply because they have a different physical constitution."

It is from Single Nucleotide Polymorphisms (SNPs) in the genome sequence that such differences arise. The human genome originally has approximately three billion base pairs, and nearly 0.1% of the sequence varies with individuals. The single difference in a base (SNP) determines the appearance, personality, and physical constitution of human beings.

"One of the most obvious examples is the difference between a heavy drinker and a light drinker," says Minami. "The distinction is caused by a certain difference in a base. We can find out whether or not the person will have a higher incidence of side effects with a certain medicine if we study the base in the same way."

Minami and his colleagues found that it was possible to determine an individual's physical constitution by examining a particular base by using a pharmacogenetics approach. They are currently conducting verification experiments to support their results.

"We are thinking about first looking at anti-cancer agents and then warfarin with its strong side effects, which is used to treat cerebral infarction. After that, we want to use the approach as an antiepileptic medication. Our goal for the future is to be able to determine what type of medicine is unsuitable for a patient within an hour after blood is drawn."

For both the utilization of hydrogen and

the attempt at tailoring medicine to patients' genetic makeup, the research underway at the institute places priority on the advantages gained for patients. Because Musashikosugi Hospital is located right next door to the institute, research results are efficiently examined in a clinical setting. Conversely, the institute immediately obtains findings and questions from clinical practice, enhancing research outcomes.

Clinicians have high expectations of their colleagues in the laboratory. Mamiko Tosa, a senior assistant professor of Musashikosugi Hospital, is an expert in the treatment of keloids, a type of fibrotic tumour formed by an overgrowth of collagen at the healing site of injury or minor skin ailments, such as a small scratch, which can seriously affect the heart. "Keloids are found only in humans, and there is no effective drug to cure this condition because we cannot conduct experiments on animals," explains Tosa. "Keloids form in certain people and not in others. At present, it is impossible to predict the constitution of keloids. Currently although keloids are removed by surgery and treated with radiation therapy for three days after surgery, nearly 20% of patients experience a recurrence of keloids."

Tosa emphasises that with no current treatments available for this serious condition, there is an urgent need to develop a constitution diagnosis and specific medicine for keloids. Tosa currently collaborates with the institute in the development of a constitution diagnosis based on genomic information. "If patients know about their predisposition to keloid formation they could avoid certain activities such as ear piercing."

Needless to say, Tosa also expects to use her achievements in keloid research to develop post-treatment methods and determine specific therapeutic treatments. Additionally, she hopes to find a way to improve the physical condition of patients based on genomic diagnosis.

"We cannot realize anything without believing. We are working positively in full coordination with the institute to aim for clinical application as early as possible" she says.

Striving to make personalised medicine a reality

While personalised medicine is an emerging area with great potential for tailor-made therapeutic treatments, some resistance still remains towards this approach.

"It is because gene information is ultimately personal information," says Minami. "Despite such opposition, we continued to work hard with the belief that the time will come when people realise the necessity of personalised medicine. As a result, I am glad that this necessity is gradually becoming recognised."

Technological advances used for analysis have also provided a boost to personalised medicine research.

"In the past, it was common practice to prepare the optimum dose for each individual. However, at some point this practice ended and the same amount of medicine began being prescribed regardless of body size. This was another reason why we wanted to provide personalised medicine as soon as possible. For example, patients' blood types are always checked before giving a blood transfusion. In the same way, the ideal situation is to clarify the possibility of side effects and the right amount of medicine for a patient before administering medication. Every effort is being made by our institute to tailor medicine to each of our patients' genetic makeup. It is the only and ultimate goal of our research. Nippon Medical School and the Institute of Development and Aging Sciences took a positive stance on personalised medicine at a time when it was too early to get people to understand. We will never change our stance in the days ahead," emphasizes Minami.

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ST. MARIANNA UNIVERSITY SCHOOL OF MEDICINE

Advanced medicine with a humanitarian spirit

Dignity of life rooted in love for all mankind is the core philosophy of the St. Marianna University School of Medicine (SMU) in Kawasaki, and one of the key benchmarks for its graduate physicians — a ‘St. Marianna Spirit’ combines broad and specialist medical knowledge with a rich humanitarian approach founded in Christianity.

Established in 1971, SMU may be unique in the world in being a specialist single-department medical college with a Christian philosophy. “We specialize in medical studies, education and care in the Christian spirit,” says school president Fumihiko Miyake. “We foster a St. Marianna Spirit of compassion in medical care by incorporating religious studies into our medical programmes to teach the fundamental frame of mind needed for those in the medical profession.”

In addition to its role in training compassionate physicians, SMU plays a central role as an advanced treatment hospital for community healthcare in Kawasaki with its Emergency Medical Care Center and Advanced Center for Perinatal Medicine, which accepts patients with difficult childbirth problems that cannot be treated at regular hospitals. This community healthcare role provides student physicians at SMU with many opportunities to gain experience in emergency and outpatient care throughout their training, through placement on Kawasaki municipal ambulances and outpatient assignments.

“In this way we give students the opportunity not only to learn the foundations of medical care but also to spend time and interact closely with patients in their community, talking about many things besides the patient’s symptoms,” says Miyake. “When our students’ assignments are complete, their patients often say, ‘I hope

you become a great doctor.’ It is an important aspect of education in the St. Marianna Spirit to teach our students the feelings of affection from patients when they provide medical care face-to-face as physicians.”

Superior medical care also involves cooperation among physicians and a range of medical and technical professions. SMU promotes the formation of effective working relationships through numerous workshops attended by professionals from diverse backgrounds, including medical doctors, nurses, laboratory technicians, physical therapists, pharmacists, nutritionists, and healthcare coordinators, under the sponsorship of the school’s Center of Interprofessional Practice & Education. These professional networks also extend to sport medicine, where the school was the first medical college in Asia and the fifth in the world to be approved as a Medical Centre of Excellence of the Fédération Internationale de Football Association (FIFA). Former president and vice-chairman of the board of directors of SMU, Haruhito Aoki, was in fact the chairman of the Sports Medical Committee of the Japan Football Association (JFA).

SMU’s designation as a university-affiliated hospital for the provision of advanced treatment allows the school to improve and develop advanced medical technologies. One of the key areas of medical technology in which the school specializes is in the treatment of infertility. The school’s Department of Advanced Reproductive Medicine under Bunpei Ishizuka, who conducted collaborative research in Obstetrics and Gynecology at the Stanford University School of Medicine in the United States, has developed the world’s first therapy for primary ovarian insufficiency using a method that involves activating dormant primordial ovarian follicles. SMU was the first in the nation to develop the ovarian tissue

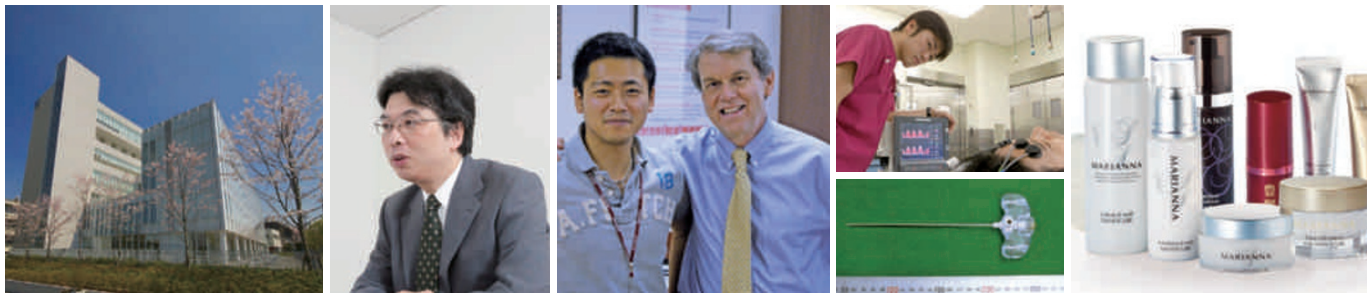


Fumihiko Miyake, President of the St. Marianna University School of Medicine.

cryopreservation techniques essential to this infertility treatment, which gives young female patients with cancer the opportunity to conceive after cancer treatment.

“We are already involved in clinical application of this ovary cryopreservation technique for pre-treatment cancer patients,” says Miyake. “We proceed with this treatment following a comprehensive determination of social ethics views and a sense of morality, while paying respect to the wishes and medical conditions of the patient who would be a mother in the future, as well as to the wishes of her family. We recognize the leading role of highly advanced medical treatment in the pursuit of the best medical care. On that basis, we respect every wish of patients and their families to determine the most appropriate treatment. The St. Marianna Spirit supports both of these elements, of technology and mind.”

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ST. MARIANNA UNIVERSITY SCHOOL OF MEDICINE, INTELLECTUAL PROPERTY MANAGEMENT CENTER

Toward universal access to advanced medical technology

Making new medical technologies available to everyone in need is the guiding principle of clinical research at the St. Marianna University School of Medicine (SMU). The school strives to utilize its new technologies and research results by translating research into clinically useful methods and through the development of commercial applications.

A key characteristic of SMU is its emphasis on finding and promoting clinical applications of the advanced medical technologies developed through research at the university hospital. The focus on clinically applicable results starts with the scope of the original study itself, which extends beyond the confines of typical basic research to encompass the development of outcomes in a form suitable for uptake by all hospitals, not just university hospitals.

A particularly successful example of this approach is the breast cancer research of Tomohiko Ohta and his colleagues in the school's Department of Translational Oncology. Through their research on the functions of the breast and ovarian cancer tumour-suppressor gene BRCA1, they discovered that the gene codes an ubiquitin E3 ligase enzyme. Their functional analysis of the BRCA1 enzyme was not just a major achievement in basic medicine — the clinical findings of those studies are now being put to use in hospitals throughout Japan as a predictive test of susceptibility to breast or ovarian cancer.

Research on the disease known as HTLV-1-associated myelopathy (HAM) is also one of the school's most significant achievements. HAM is a viral infection of the spinal cord that causes leg weakness and eventually the inability to walk. It is estimated that more than 20 million people worldwide, primarily in developing countries, may be infected with the HTLV-1

virus responsible for this disease, and there are nearly 3,000 known HAM cases in Japan. The Department of Rare Diseases Research in SMU's Institute of Medical Science has established a division exclusively for HAM patients and for development of innovative new drugs for treating the disease under the direction of Yoshihisa Yamano.

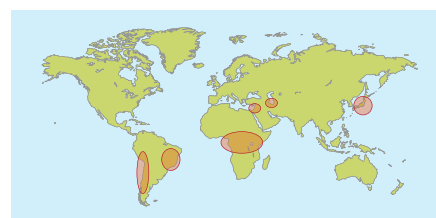
"We are driving our HAM research as an area in which Japan could lead the world," says Noboru Suzuki, director of the Intellectual Property Management Center in the SMU. "The school aims to establish a global base in the field of HAM with a view to collaborating with international research institutes on joint clinical trials for HAM therapies."

SMU is actively engaged in the application and dissemination of medical technologies developed through the school's activities in corporation with the technology transfer organization, MPO Inc. which is fostering business and venture opportunities surrounding these technologies.

A bone cement injection puncture needle developed by Kenji Takizawa of SMU's Department of Radiology, for example, has recently been submitted as an international patent and is undergoing development as a standard clinical tool for the treatment of painful compression fractures of the spine caused by osteoporosis or malignant bone tumors.

A device designed by Yasuaki Koyama of SMU's Emergency and Critical Care Medicine Division for real-time measurement of cerebral blood flow during cardiopulmonary resuscitation is another new technology developed at SMU and one with considerable promise in emergency care. The device is undergoing further development with the integration of near-infrared spectroscopy and is expected to become commercially available within the next few years.

Kihei Yoneyama of the Division of Cardiology



The worldwide distribution of HTLV-1 cases.

in the Department of Internal Medicine has invented a new type of cardiac computed tomography (CT) scan that utilizes imaging data previously not considered in such diagnostics. In collaboration with Toshiba Medical Systems Corporation, the SMU's cardiac CT scan is being developed as a high-integrity diagnostic method that offers lower medical radiation exposure.

Yet another achievement of the school is the university-launched venture company NANOEGG Research Laboratories, Inc., an enterprise specializing in drug development and cosmetics. Under the direction of Yoko Yamaguchi of the Department of Rare Diseases Research in SMU's Institute of Medical Science, NANOEGG is developing a medical cosmetics line called MARIANNA based on nanocapsule technology used in drug delivery. With no precedent for the use of drug delivery technology in cosmetics, the MARIANNA cosmetic line is pioneering a new market. "The skin is an important organ and just like drugs and medicines, it is becoming increasingly important for experts to develop cosmetic products through a process that involves the verification of both advantageous and adverse effects," says Suzuki.

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MEIJI INSTITUTE FOR ADVANCED STUDY OF MATHEMATICAL SCIENCES (MIMS)



Making an impact with mathematical sciences

Novel approaches to mathematical modelling and analysis are being developed at Meiji University to address new challenges in previously unexplored areas.

Founded in 1881, growth of Meiji University's is closely linked with the history of Japan's modernisation. At the leafy Ikuta Campus in Kawasaki, undergraduate- and graduate-level students and researchers are involved in diverse fields of science and engineering.

As an integral part of the Ikuta Campus, the Meiji Institute for Advanced Study of Mathematical Sciences (MIMS) has distinguished itself as a top-level international research centre pursuing mathematical analyses of various natural and social phenomena.

Masayasu Mimura, director of MIMS, comments: "Our goal is to develop mathematical sciences that contribute to society. Advances in experimental and observational techniques have enabled us to access a large body of data. We have also achieved a profound understanding of the individual components. However, it may be more important to analyse interactions rather than to track individual movements when probing the causes of a wide range of phenomena, such as disease epidemics, the instability of the financial sector, and traffic congestion. As an example, human genome sequencing alone will not yield the 'whole picture' of a system as complex as the human body. To move from studying the components that make up a system toward a deeper understanding of the bigger picture, mathematical sciences have a significant role to play in this transition."

Mimura also serves as project leader of the Global Center of Excellence (GCOE) Program titled 'Formation and Development of Mathematical Sciences Based on Modelling and Analysis', approved in 2008 by Japan's Ministry of Education, Culture, Sports, Science, and Technology (MEXT).

A specialist in mathematical modelling, Mimura himself coined the term 'mathematical modelling and analysis', which covers various aspects of modelling, mathematical analysis and simulation. Mimura's applied approach had at times been viewed as unconventional within the Japanese mathematical community, due to the importance it placed on the study of pure mathematics. The establishment of MIMS in 2007 marked a milestone in the development of a more diverse research environment.

Modelling visual illusions

Kokichi Sugihara, a deputy director of MIMS, is renowned for his work on illusory mechanisms involved in human perception and cognition, and has developed the field of 'computational illusion', whereby mathematical models can help to explain the basis of different perceptual processes.

"I brought mathematics into the field of perceptual illusion — an area that used to be the domain of psychologists and cognitive scientists," Sugihara explains. "We study the mechanism of perceptual illusion by developing mathematical models of the eye, which are thought to cause such illusions. In this way, we may be able to describe the parameters of illusion in numerical terms, and thus optimise and control these illusory perceptions." Accidents often arise as a result of perceptual illusions. By designing environments that are least likely to produce illusions, it may be possible to build a safer society. "And in contrast, we could also make road signs that are difficult to miss by 'strengthening' illusions," Sugihara adds. "We can contribute to society by applying computational illusion methods — by adjusting the strength and weakness of various illusions."

Origami engineering

Based on his background in mechanical engineering, Ichiro Hagiwara, another deputy director of MIMS, has collaborated with Taketoshi

Nojima of Kyoto University to establish a unique field of study called 'origami engineering'. Hagiwara says, "In Japan, there are many great origami artists, and their work is based on aesthetics — in other words, it is an artform. Recently, researchers outside Japan have popularised the geometry of origami and have even industrialised it. A British engineer developed a honeycomb structure based on decorations for the traditional Japanese 'Tanabata' festival, and it has grown to an industry worth tens of billions of dollars. We are working on new Japanese origami engineering to promote new industrial applications." Hagiwara's proposals include non-honeycomb structures based on metallic and other materials. He envisages applications in a wide variety of fields, including solar panels and the development of a new type of automobile bumper capable of absorbing energy on crash.

Education and collaboration at MIMS

Through its GCOE program, MIMS is setting up PhD scholarships, to attract high-calibre students from around the world. "Traditionally, we have a wealth of outstanding mathematicians in the country," says Mimura. "We aim for MIMS to be a melting pot of mathematical ideas. To this end, one of our top priorities is education."

MIMS is also engaged in research collaborations with institutions in Japan and abroad. "We are currently collaborating with the Centre for Mathematical Biology at the University of Oxford in the UK and the National Centre for Scientific Research in France," says Mimura. "We are planning to build on our global collaborations that leverage the strength of each partner."

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MEIJI UNIVERSITY INTERNATIONAL INSTITUTE FOR BIO-RESOURCE RESEARCH (MUIBR)



Shaping our future with cloned and transgenic pigs

The development of transgenic pigs has generated widespread interest due to the ways in which they may be used for the development of human disease models and for providing organ transplants.

The Meiji University International Institute for Bio-Resource Research (MUIBR) is a leading international research institute that focuses on translational research in the fields of rare and incurable diseases, organ transplantation and regeneration, and reproductive medicine. Hiroshi Nagashima, director of MUIBR, is also a professor at the school of agriculture, Meiji University, and one of the front-runners in the study of somatic cell nuclear transfer (SCNT) pig clones and transgenic pigs. In November 2009, Nagashima successfully cloned sixth-generation pigs based on the SCNT technique.

On the growing interest in cloning technologies, Nagashima notes, "Pigs' organs are comparable in size to human organs. Also, pigs are omnivorous, and so the structure and physiology of the pigs' digestive system are similar to that of humans. From the 1990s, there has been increasing interest in genetically-engineered livestock for medicinal use, and there has been a corresponding interest in cloned and transgenic pigs."

Developing disease models

By applying SCNT technology, developing animal models for various human diseases has been made possible. Nagashima created the world's first pig model of diabetes by nuclear transfer of a somatic cell transfected with mutant human hepatocyte nuclear factor-1 α (HNF-1 α) gene into a pig egg. The gene causes maturity onset diabetes of the young type 3 (MODY3). "This pig model is useful for the development of diabetes drugs, new therapies, and preclinical research into regenerative

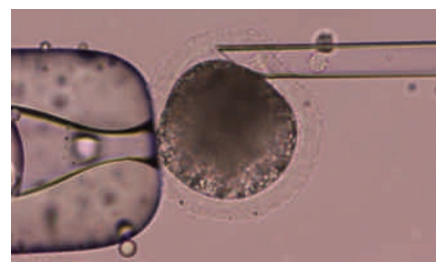
medicine," says Nagashima. "The technique can also be applied to other intractable and rare diseases."

Nagashima and his colleagues are also embarking on efforts to address cross-species organ regeneration. The ultimate goal of this work is to produce a genetically engineered pig that does not possess a pancreas, and then use the empty space or 'niche' in the body to grow a viable pancreas from human induced pluripotent stem cells (iPS cells). Nagashima comments, "We have already created a pig without a pancreas. Since we are not allowed to inject human cells into fertilised pig eggs under current Japanese law, we will use iPS cells of cows and monkeys to demonstrate that organ regeneration is possible between large animal species."

Research at the MUIBR is being carried out in collaboration with the University of Munich in Germany, the National Swine Resource and Research Center (NSRRC) at the University of Missouri in the US, Yunnan Agricultural University in China, and Seoul National University in South Korea, as well as with several organisations in Japan.

Archiving genetic resources

The successful creation of a gene bank has been a long-standing challenge for the development of transgenic and cloned pigs as genetic resources. Fertilised pig eggs are vulnerable to low temperatures and freezing them is more complicated than preserving the eggs of other types of livestock. In view of these challenges, Nagashima and his co-workers developed a technique called 'hollow-fibre vitrification' for *in vitro*-matured and -fertilised eggs. Nagashima says, "We found that the hollow fibre for artificial blood filtration commonly used in dialysis machines would make an excellent device for freezing pig eggs. We use the



Somatic cell nuclear transfer: A genetically modified pig cell about to undergo nuclear transfer into a pig egg without a nucleus.

hollow fibre to make a capsule about one to two centimetres long, into which we place a few dozen fertilised eggs. The eggs are vitrified instantaneously. Using this technique, the cell survival rate is quite high."

Another world-first developed by Nagashima's team is the 'red fluorescent pig' created by transfection with a red fluorescent protein (RFP) gene. While green fluorescent protein (GFP) is well-known, Nagashima explains that "red has a higher wavelength than green and is better at tracing and imaging grafted cells." The red fluorescent pig can be used as a useful model to track the reconstruction of ligaments after transplantation.

Based on these novel technologies, Nagashima envisions a bright future for medicinal research. "We aim for as many people as possible to be able to use the animal models we have already created as a research platform. In addition, we hope to contribute developing disease models for rare and incurable paediatric diseases."

Meiji University International Institute for Bio-Resource Research
<http://muiibr.com/english/index.html>



SHOWA DENKO K.K. KAWASAKI PLANT



State-of-the-art recycling and innovative technologies

As a leading supplier of diverse and unique chemical products to a wide range of industrial sectors, Showa Denko's Kawasaki Plant has world-class recycling capabilities to maximise efficiency and promote the most advanced 'waste-free' recycling methods.

Built on a vast 559,000-square-metre site in Kawasaki City, the Showa Denko (SDK) Kawasaki Plant is one of the largest of SDK's nationwide network of industrial plants, and acts as a centre for the development and production of organic and inorganic chemicals. Showa Denko was established as Showa fertiliser in 1928, and just three years later, the production of ammonia and ammonia sulphate for agricultural fertiliser was initiated at what would later become the Kawasaki Plant.

"We were the first to succeed in manufacturing ammonia and ammonia sulphate based on a process developed by the then Government Chemical Industrial Research Institute in Tokyo, later reorganised into the National Institute of Advanced Industrial Science and Technology (AIST). At that time, all of our competitors were using technologies licensed from abroad," says Taichi Nagai, plant manager of the SDK Kawasaki Plant.

Showa Denko has since gone on to diversify its products year on year; today, the SDK Kawasaki Plant boasts a product line-up of nearly 100 items including ammonia, caustic soda (sodium hydroxide), sodium hypochlorite and other basic chemicals used as raw materials for many useful products. The SDK Kawasaki Plant product portfolio also includes a wide variety of gases such as nitrogen, hydrogen, oxygen and other industrial gases, as well as high-purity ammonia, chlorine and other high-purity gases required for the production of semiconductors, liquid crystals, solar cells, light-emitting diodes (LEDs), and specialty chemicals including food

additives and materials for cosmetics.

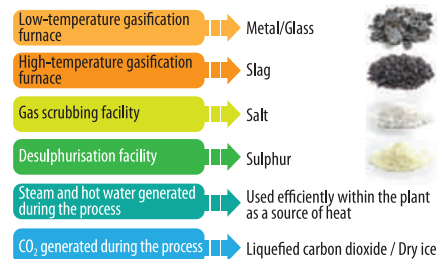
Today, Showa Denko is also engaged in developing products and technologies relating to the energy, environment, and the information and electronics business domains. One of the most notable environment-focused activities at the Kawasaki Plant is the production of ammonia from used plastics. Central to this technology is the 'zero-emission used plastics chemical recycling plant' housed within the Kawasaki Plant. The recycling plant is capable of extracting hydrogen — one of the raw materials for the manufacture of ammonia — from plastic bags, shampoo bottles, and other household waste plastics. Standing 60 meters high, the recycling facility is one of the largest in Japan and is capable of processing 64,000 tonnes of waste plastics annually.

Recycling with an environmental focus

Nitrogen and hydrogen are indispensable to ammonia production. Although nitrogen from the atmosphere is readily available, the process of hydrogen production has had a long and complex history. Around 1931, the primary method for producing hydrogen was through electrolysis of water and later on from the processing of petroleum, naphtha and natural gas. After many years of efforts to identify cost-effective raw materials that minimise harmful environmental impacts, waste plastics have been found to be favourable source materials for hydrogen production.

"Waste plastics contain large amounts of hydrogen and carbon. After thorough decomposition, we extract hydrogen as a raw material for ammonia, and carbon as a raw material for carbon dioxide (CO₂). The CO₂ emissions for the entire supply chain have now been reduced to about a half compared with conventional production processes," Nagai explains.

The recycling facilities at the Kawasaki Plant



Zero-emission recycling: Almost all by-products emitted during the production are recycled.

are based on a two-stage process: First, waste plastics are crushed and then moulded so as to reduce their volume. Next, the plastics are gasified in a two-stage gasification furnace that, remarkably, produces no harmful emission gases such as dioxin. During this stage, the plastics are processed in a low-temperature gasification furnace at 600 to 800 degrees Celsius. The resulting gas is reformed into synthetic gas, consisting mainly of hydrogen and carbon monoxide in a high-temperature gasification furnace at 1,400 degrees Celsius. Finally, hydrogen can be extracted and go on to be combined with nitrogen to produce ammonia at a neighbouring plant.

Other elements and materials such as carbon, salt, sulphur, slag, metal and glass can also be recovered in this process. The Kawasaki Plant is equipped to convert salt to caustic soda, and sulphur can be made into many useful sulphur derivatives. Nagai says waste materials are rarely disposed of without yielding useful materials.

"The high recycling rate is the biggest advantage of our recycling method. Moreover, the heat generated during the operation of the recycling plant can be used by another plant, and we are planning to expand this heat recycling capability. The steam required to operate the recycling plant is generated by another plant within our facilities, so the entire Kawasaki Plant acts rather like a single ecosystem."



When the recycling plant went into full-scale operation in 2003, SDK faced a number of challenges, such as the management of waste plastics collected and brought into the plant site by regional municipalities, the removal of various substances mixed into waste plastics, and the corrosion of plant facilities by the hydrochloric acid generated from polyvinyl chloride. These challenges have been addressed and overcome by SDK one by one.

Currently, the volume of ammonia produced at the recycling plant accounts for about one-third of the total annual output of 100,000 to 120,000 tonnes at the Kawasaki Plant. The ammonia can be used not only as raw material for acrylic fibres, nitrogen fertilisers, adhesives and clear resins, but also in environmentally-focused activities, such as the removal and scrubbing of nitrogen oxides generated at fossil-fuel-fired power stations, and for use as alternatives to chlorofluorocarbons (CFCs). The ammonia produced at SDK, named ECOANN®, was selected by Kawasaki City as a 'Low-CO2 Kawasaki Pilot Brand' in February 2012. There are plans to increase the proportion of ECOANN® in SDK's total ammonia production.

Looking to the future, Nagai comments: "We are not just focusing on waste plastics — our recycling plant can gasify other materials, and we are looking into the possibilities of recycling organic wastes, such as those generated from plants in the petroleum industry."

Cutting-edge analytical equipment

Another area in which the SDK Kawasaki Plant has produced signature technologies is high-performance liquid chromatography, a technique that is also contributing to SDK's activities in the energy and environment business field.

"High-performance liquid chromatography is used for the separation and analysis of chemical substances. It is a useful tool to analyse the

composition of various compounds. A long, thin cylindrical column with a diameter ranging from several millimetres to several centimetres is used to separate a sample. This column is essential to high-performance liquid chromatography — the degree of analysis is dependent on column performance," says Katsuyuki Tsuji, general manager of the Chemicals Development Department.

When a liquid sample is poured into the column, the sample separates into its constituent components. Each of the components moves through the column at a different velocity, and can be extracted according to different retention times. For example, when orange juice is introduced into the column, the components can be extracted in the following order: cane sugar, glucose, and fructose.

"The Kawasaki Plant manufactures a diverse range of polymers that can be used to fill the column. After injecting the filler into a stainless steel tube, we ship the finished column to market," Tsuji explains. "Currently, we are focusing on improving and expanding the range of column products that can be used in energy and environment-related fields. We aim to improve and increase production of our columns not only for universal use, but also to develop specialised ones that yield excellent results in the analysis of the so-called 'sugar system', which is important for the production of bioethanol. These columns are particularly effective in the analysis of water."

The columns produced by SDK bear the trade name Shodex®. The market share of Shodex®-branded columns today has reached nearly 50% in Japan, and SDK also boasts a substantial share of the global market, ranking as one of the top three global manufacturers of these products.

Expansion of overseas activities

In the information and electronics field, SDK is expanding its overseas business operations

Silicon semiconductor		Compound semiconductor		
C ₂ F ₆	c-C ₄ F ₈	CH ₂ F ₂	C ₄ F ₆	BCl ₃
N ₂ O	CH ₃ F	C ₃ F ₈	CHF ₃	HBr
Liquid crystal		HCl		
Solar cell	SF ₆	NH ₃	COF ₂	Cl ₂
		NF ₃	CF ₄	H ₂ Se

Electronic material gas products: Process material gases required in the electronic industry can be offered in large quantities.

based on high-purity gas manufacturing technologies developed at the Kawasaki Plant so as to respond to increasing demand for high-purity gases, particularly in the East Asia region. Elsewhere in Asia, SDK has manufacturing facilities in China, South Korea and Taiwan.

"High-purity gases are essential to the production of semiconductors and liquid crystals used in various devices, as well as environmentally-friendly technologies such as solar cells and LEDs. High-purity ammonia gas is important for the production of these devices," says Tsuji.

Foreseeing the rapidly increasing demand for gallium nitride semiconductors, which are a vital component for the production of white LEDs that have remarkable energy-saving properties, SDK has been engaged in efforts to improve on the technology to manufacture high-purity ammonia required to produce these semiconductors. In 2011, SDK succeeded in increasing the annual output of high-purity ammonia from about 3,000 tonnes to 5,000 tonnes.

The SDK Kawasaki Plant continues to make great strides in developing innovative manufacturing technologies to accelerate the development of high-quality materials and components based on SDK's state-of-the-art technologies and sound expertise.

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KANAGAWA SCIENCE PARK AND KSP, INC.

At the forefront of industrializing research and development

For the past quarter century, Kanagawa Science Park and KSP, Inc. have continuously fostered unique venture companies.

At the end of the 1970s, the promotion of high added value production became an important theme within the Keihin Industrial Zone, and instigated various proposals to open Japan's first science park in Kanagawa. KSP, Inc., the core company of the Kanagawa Science Park, was established first in 1986, and the science park followed in 1989. Since that time, KSP, Inc. has made great advances in the incubation and development of emerging R&D ventures.

While the Kanagawa Academy of Science and Technology (KAST) is responsible for research support, KSP, Inc. takes the lead in the industrialization and commercialization of new technologies. A prime example is the biotech company, LivTech, Inc. which was established by primary researchers from KAST with support of KSP, Inc. after the completion of the five-year Stem Cell Regulation Project. Today LivTech plays an important role in the research and development of antibody drugs for the treatment of cancer.

Framework for realizing incubation

"KSP, Inc. offers support for emerging venture companies from three aspects: by providing research facilities, project funds through investment, and support services, such as KSP Business Innovation School (KSP-BIS) and business match-making," explains Tomoyoshi Okita, KSP, Inc. president and representative director. "For example, when venture companies are established by researchers, KSP, Inc. is continuously involved in diverse ways from planning to business operations, such as taking equities or providing research facilities without making an investment."

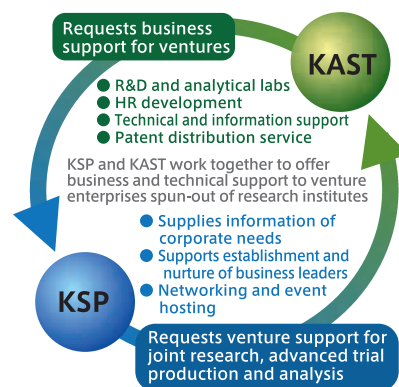
According to Okita, in recent years an increasing number of researchers have started venture companies after graduating from KSP-BIS. One example is NANOEGG Research Laboratories, Inc., a venture company established by researchers from the St. Marianna University School of Medicine. NANOEGG produces and sells cosmetics using nanoencapsulation technologies. TagCyx Biotechnologies, Inc., and AAC Laboratories, Inc., which are venture companies originating from the RIKEN Yokohama Institute in Yokohama, are also companies created by graduates from KSP-BIS. TagCyx Biotechnologies was established in 2007 using the technology of a man-made base pair system for the expansion of genetic information, while AAC Laboratories develops testing for allergens and the strength of allergies in canines, which are mainly available to veterinary surgeons.

Cutting edge R&D facilities

Kanagawa Science Park houses approximately 50 venture companies and 70 major companies both domestic and overseas. Most of these companies use the science park as a base for research and development.

"Unlike regular office buildings, Kanagawa Science Park is fully equipped with facilities intended for corporate research and development," says Okita. "There are many benefits to conducting research and development at the science park. For example, we are able to set up clean rooms in the building, which is also equipped with central wastewater treatment facilities and a floor weight capacity designed for large-sized equipment and large-capacity electrical equipment. No other facility in Japan is as completely equipped with the most appropriate environment for research and development, along with accessibility within 30 minutes by train from downtown Tokyo.

Collaborative mechanism for the expediting of research spin-off venture companies



Although there are some restrictions on experiments using animals due to its location in an urban district, if necessary, we offer referrals to use facilities in the Keihin Rinkai zone as a flexible response to research and development needs in various fields."

KSP, Inc. has invested capital in approximately 100 venture companies, and of them, seven companies have conducted initial public offerings (IPO). After the Lehman collapse in 2008, the number of venture companies executing an IPO in emerging markets declined. However, in 2011, the market saw improvement, and three venture companies funded by KSP, Inc. went public. Okita emphasized his commitment to supporting venture companies. "In the future, we hope to see not only more initial public stock offerings, but the acquisition of businesses and the technologies developed by venture companies released as products onto the world market."

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KANAGAWA ACADEMY OF SCIENCE AND TECHNOLOGY



Promoting Kanagawa's advances in science and technology to the world

Based at the Kanagawa Science Park in Kawasaki City, and established in 1989, the Kanagawa Academy of Science and Technology (KAST) plays a pivotal role in regional development in Kanagawa by nurturing creative research projects and providing key technological support to various universities, research institutions, and corporate laboratories.

KAST's key mission is to bring cutting-edge research and technology from Kanagawa to the international stage. KAST also facilitates technology transfers, cultivates personnel to oversee scientific and technological progress, and supports small and medium businesses in the Kanagawa region with the aim to revitalize the local economy and improve quality of life.

In particular, KAST strongly promotes research projects in collaboration with sectors of industry, academia, and government, and aims to employ the power of science and technology to solve regional challenges and stimulate industries.

In recent years, KAST has embarked on pioneering work in advanced science and technology fields such as the biosciences in line with its strategy for international development. KAST has also conducted collaborative research and development with the goal of establishing performance evaluations and certification criteria in anticipation of market deployment.

Developing methods for evaluating food functionalities using a nutrigenomics approach

Functional foods research in Japan has made great strides since the concept of physiologically functional foods was introduced by Japanese researchers in a news article in *Nature* back in 1993. Now in 2012, a major initiative known as the Project on Health and Anti-Aging, headed by Keiko Abe, emeritus professor at The University of Tokyo, is being promoted by KAST. The project takes a scientific approach to evidence-based evaluative analysis of the effect and efficacy of functional food and cosmetics for health and anti-aging, and strives to further the development of wellness products through key collaborations with several Kanagawa-based food and cosmetic corporations.

Diet and lifestyle are thought to have a major impact on an individual's susceptibility to disease. A healthy diet is essential to quality of life and the prevention of lifestyle-related illnesses, such as stroke, heart disease and obesity. In Japan, the number of those aged 65 or older is expected to soon reach 30 percent of the

total population, and the development of functional foods to maintain wellness now plays a critical role in finding ways to delay the onset of lifestyle-related diseases associated with aging.

In earlier research, the analysis of the effects and efficacy of functional foods was carried out in a non-holistic fashion. However, by harnessing DNA microarray chip technology, researchers have succeeded in applying a nutrigenomics approach to make predictions at the genetic level and to thoroughly analyze the biological activity and functions of foods and food constituents.

Nutrigenomics is an emerging field that investigates the effect of foods and food constituents on gene expression, employing experimental and data analysis and high-throughput genetic screening techniques to further explore the effect of nutrients on genes in the human genome. To properly interpret the results of nutrigenomics, it is important to focus on genomics (transcriptomics) combined with omics technologies, such as proteomics and metabolomics.

The development of wellness and anti-aging



Keiko Abe, leader of the Project on Health and Anti-Aging.

products, in particular, requires demonstrating broad-based scientific evidence by taking an evaluative analysis of its effects and efficacy in a holistic way. The project's nutrigenomic approach validates the biofunctions of products and aims to apply the results to basic research in human studies.

Furthermore, unlike pharmaceuticals, unsafe foods and cosmetics generally do not produce acute symptoms or effects, making identifying them correspondingly more problematic.

As well as promoting the benefits of a collaborative approach, this project also strives to lead the way in establishing a public independent evaluation organization for the development of scientific evidence-based wellness and anti-aging products, and a centre for international certification standards development and evaluation.

Through the Project on Health and Anti-Aging and other collaborations with institutions and industrial sectors, KAST will continue to spearhead new scientific and technological solutions to advance food functionality research and the development of wellness and anti-aging products, and to deliver key innovations in science to the world stage.

Kanagawa Academy of Science and Technology

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